JVIN Journal of Vascular and Interventional Neurology
OFFICIAL JOURNAL OF THE ZEENAT QURESHI STROKE INSTITUTE

Institution of Code Neurointervention and Its Impact on Reaction and Treatment Times

Spozhmy Panezai, MD[*,1], **Sanket Meghpara, MD**[2], **Ashish Kulhari, MD**[1], **Jaskiran Brar, MD**[3], **Laura Suhan, NP-C**[1], **Amrinder Singh, MD**[1], **Siddhart Mehta, MD**[1], **Haralabous Zacharatos, MD**[1], **Sara Strauss, MD**[1], and **Jawad Kirmani, MD**[1]

[1]*JFK Stroke and Neurovascular Center, Hackensack Meridian Health-JFK Medical Center, Edison, NJ USA*

[2]*Tripler Army Medical Center, HI 96859*

[3]*Surrey Memorial Hospital, B.C, Canada*

Abstract

Background/Objective—Various strategies have been implemented to reduce acute stroke treatment times. Recent studies have shown a significant benefit of acute endovascular therapy. The JFK Comprehensive Stroke Center instituted Code Neurointervention (NI) on May 1, 2014 for the purpose of rapidly assembling the NI team and rapidly providing acute endovascular therapy.

Design/Methods—We performed a retrospective analysis of all patients who had Code NI (Code NI group) called from May 1, 2014 to July 30, 2018 and compared them to patients who underwent acute endovascular treatment prior to initiation of the code (pre-Code NI group) between January 2012 and April 30, 2014. The following parameters were compared: door to puncture (DTP) and door to recanalization (DTR) times, as well as preprocedure NIHSS, 24-hour postprocedure NIHSS, and 90-day modified Rankin scores.

Results—There were 67 pre-Code NI patients compared to 193 Code NI patients. Mean and median DTP times for pre-code NI vs Code NI patients were 161 minutes(mins) vs 115mins ($p<0.0001$, 31.76-58.86) and 153mins vs 112mins ($p<0.0001$), respectively. Mean and median DTR times were 220 mins vs 167mins ($p<0.0001$, 37.76-69.97) and 225mins vs 171mins ($p<0.0001$). Mean pre-procedure NIHSS was 16 for both groups while 24 hours post procedure NIHSS was 10.6 vs 10.8 ($p=.078$, 1.8-2.38). Mean 90 day mRS was 2.15 vs 1.65 ($p=0.036$, 0.32-0.96).

Conclusion—Institution of Code NI significantly improved DTP and DTR times as well as mRS at 3-months postprocedure. Rapid assembly of the NI team, rapid availability of imaging and angiography suite, and streamlining of processes, likely contribute to these differences. These lessons and more widespread institution of such codes will further aid in improving acute stroke care for patients.

Introduction

Stroke is a leading cause of serious long-term disability and the fifth leading cause of death in the United States [1]. Ischemic strokes, in which blood flow to the brain is blocked, account for about 87% of all strokes [2]. The longer neuronal tissue is without adequate blood flow, the greater the extent of damage to the brain [3]. Thus, time plays an important role in predicting clinical outcomes and treatment effect in cerebral ischemia and further supports the need for emergent assessment and treatment.

Although stroke continues to impact the population heavily, stroke care overall has improved in many ways. This is likely due to many factors including better primary and secondary prevention and more rapid and effective acute stroke treatments [4]. Intravenous alteplase (IV tPA) continues to be the only FDA approved medical treatment of acute ischemic stroke; however, outcomes with treatment are time-dependent. A large meta-analysis of individual patient data from randomized clinical trials showed that the odds ratio (OR) for a good outcome was 1.75 for treatment within 3 hours of

Vol. 11, No. 1, pp. 1–5. Published January, 2020.

***Corresponding Author:** Spozhmy Panezai MD, JFK Stroke and Neurovascular Center, Hackensack Meridian Health-JFK Medical Center, 65 James St, Edison, NJ 08820, USA. Tel:(732)744-5805. spozhmy.panezai@hackensackmeridian.org

stroke onset and 1.26 for treatment between 3 and 4.5 hours; the absolute benefit decreased from 9.8% to 4.2% in these time windows [5].

Various strategies have been undertaken to reduce acute stroke treatment times, including institution of a Code Stroke alert and improvement of door to CT and door to needle times [6,7]. In contrast to the IMS III, MR RESCUE, and Synthesis Expansion trials, which failed to show improved outcomes with endovascular therapy, more recent studies (MR CLEAN, EXTEND IA, ESCAPE, and SWIFT PRIME) have shown a significant benefit of endovascular therapy in acute stroke treatment [8–12]. Earlier reperfusion (within a 6-hour window) of large vessel occlusions (LVOs) via intraarterial treatment has been shown to correlate with improved outcomes [13–15]. In fact, with the use of advanced neuroimaging techniques and careful patient selection, acute endovascular thrombectomy has been shown to be feasible and results in better patient outcomes when performed up to 24 hours of last known well time [16]. In addition, a meta-analysis by the HERMES Collaborators has shown that shorter emergency department (ER) arrival to groin puncture time period was associated with higher recanalization rates of occluded vessels and better clinical outcomes [17,18].

In May 2014, the Hackensack Meridian JFK Comprehensive Stroke Center instituted a Code Neurointervention (NI) process for the purpose of rapidly assembling the NI team and rapidly providing acute endovascular treatment. This alert was set up in addition to the already existent Code Stroke alert. Door to puncture (DTP) and door to recanalization (DTR) were compared to corresponding times from the years prior to institution of Code NI. Preprocedure and 24 hours postprocedure NIHSS Scores were compared as well as 90-day mRS. These time measures will continue to be looked at in more detail to see where further improvements in the process can be made.

Method

A Code Stroke alert was already in place to activate the stroke team for the purpose of rapid patient assessment and stabilization, imaging acquisition, and administration of IV tPA to eligible patients. Prior to institution of Code NI, the acute stroke team would first have a discussion with the neurointerventionalist on call as to whether a patient would be a candidate for neurointerventional treatment. This was based on the patient's clinical presentation, advanced imaging modalities (CT, CT angiography, and CT perfusion), and physician recommendation. If it was felt that the patient may benefit from a procedure, then the entire neurointerventional team (physicians, technicians, and nurses) would personally be notified by the stroke team and called in after hours. Delays to treatment in this paradigm included extra time needed for acquisition and interpretation of advanced imaging, discussion with the neurointerventionalist, and notification of the individual members of the team, as well as travel time if the team was not in house after hours and on weekends, and patient preparation prior to groin puncture. Time metrics, including door to decision for NI, DTP, and DTR were reviewed in early 2014. It was determined that improvements needed to be made in order to make the process more efficient and timely.

A process improvement project was undertaken by the multidisciplinary stroke team in early 2014 and a Code NI alert and policy were created for the purpose of rapid activation of the NI Team. Under this new policy, the stroke team made the determination as to whether a patient would be a candidate for NI and the team would activate the Code NI prior to speaking with the neurointerventionalist. The NI team members were provided with pagers through which they would be alerted simultaneously. The patient was prepared for the procedure in the emergency room and was brought to the neurointerventional suite as soon as the room was available and a technician arrived. The emergency room nurse would care for the patient and would remain to start the procedure until handoff was given to the interventional nurse. The patient's groin was prepared and draped and the neurointerventionalist would puncture upon arrival. Education was given to the various staff that would be involved in this process (including the ED, radiology, neurology, stroke, and ICU staff) and an official hospital-wide policy was created and approved by administration. On May 1, 2014, this alert was officially instituted and time parameters were collected.

We performed a retrospective analysis of all patients who had Code NI called from May 1, 2014 to July 30, 2018 and compared them to patients who underwent acute endovascular treatment from January 1, 2012 to April 29, 2014, the years prior to initiation of the new code(pre-Code NI). The following time parameters were compared: DTP and DTR times. Preprocedure and 24-hour postprocedure NIHSS and 3-month postprocedure Modified Rankin Scores were also compared between the groups to see if institution of the new process resulted in better outcomes.

Statistical analysis was performed using the GraphPad QuickCalcs Web site. A two-tailed *t*-test was performed.

Journal of Vascular and Interventional Neurology, Vol. 19

Table 1. Pre-Code NI versus Post-Code NI data

	Pre-Code NI	Post-Code NI
Door to groin puncture		
No. of patients	67	193
Mean	161	115
Median	153	112
P-value, 95% confidence interval (CI)	<0.0001 (32.06–58.55)	
DTR		
No. of patients	67	193
Mean	220	167
Median	225	171
P-value, 95% CI	<0.0001 (38.15–69.58)	
mRS on discharge		
No. of patients	67	193
Mean	3.98	3.91
Median	4	4
P-value, 95% CI	0.7238 (–0.29 to 0.42)	
3-month mRS		
No. of patients	67	193
Mean	2.15	1.65
Median	2	1
P-value, 95% CI	0.0361 (0.032–0.95)	
Initial NIH		
No. of patients	67	193
Mean	15.70149254	16.08854167
Median	15.5	17
24-hour NIH		
No. of patients	67	193
Mean	10.6	10.8
Median	11	10
NIH change		
No. of patients	67	193
Mean	5.45	5
Median	5	4
P-value, 95% CI	0.6621 (−1.59 to 2.5)	

Results

There were 1008 total ischemic stroke patients admitted to the hospital during the pre-Code NI period versus 2255 total ischemic stroke patients in Code NI time frame. Of these, there were 67 patients who underwent NI in the pre-Code NI period compared to 193 NI patients in the Code NI time frame (Table 1). Mean and median DTP times for pre-Code NI versus Code NI patients were 161 mins versus 115 mins ($p < 0.0001$, 31.76–58.86) and 153 mins versus 112 mins ($p < 0.0001$), respectively. Mean and median DTR times were 220 mins versus 167 mins ($P < 0.0001$, 37.76–69.97) and 220 mins versus 171 ($p < 0.0001$). These reductions in response and treatment times were statistically significant. Mean preprocedure NIHSS was 16 for both groups while 24 hours postprocedure NIHSS was 10.6 versus 10.8 ($p = 0.078$, 1.8–2.38). This was similar in both groups. The change in NIHSS preprocedure and 24 hours postprocedure in both groups was the same as well and was not significant. Mean 90-day mRS was 2.15 versus 1.65 ($p = 0.036$, 0.32–0.96) which was statistically significant.

Discussion

The outcomes of patients with LVOs heavily depend on the time from stroke onset to recanalization of the occluded vessel. Major criticisms of the IMS III, MR RESCUE, and Synthesis expansion trials included not only the usage of older devices but also the prolonged duration of time between stroke onset and initiation of endovascular therapy. Median time from stroke onset to groin puncture in MR RESCUE, IMS III, and Synthesis expansion was 330, 212, and 245 minutes, respectively [8,19,20]. As a result, recanalization rates were lower and endovascular therapy was concluded to be inferior to IV thrombolysis. Although a big portion of such time delays includes stroke recognition and ED presentation, a large amount of time is also spent between ED arrival to initiation of endovascular therapy.

The meta-analysis by the HERMES Collaborators showed that the time between stroke onset to ED arrival did not significantly effect clinical outcomes post thrombectomy. However, pronounced treatment effect modification was observed with various time metrics beginning from ER arrival [17]. One possible explanation for this includes imprecise determination or documentation of stroke onset time compared to more accurate ED arrival time [21]. A sigmoid trajectory of cerebral injury following ischemia, with most of the damage happening in the intermediate time period after stroke symptom onset rather than early after stroke onset may also explain such findings [3,22].

The HERMES Collaborators concluded that for every 1000 LVO patients achieving substantial endovascular reperfusion and for every 15-minute more rapid ED door to reperfusion times, an estimated 39 patients would have better outcomes at 3 months. This included 25 more patients who would achieve functional independence (mRS 0–2) without any significant difference in rates of mortality, symptomatic intracranial hemorrhage, and major parenchymal hematoma [17]. Rates of functional independence at 3 months declined with delays in symptom onset to reperfusion time same as: age, baseline stroke severity, clot location, initial extent of cerebral infarction (ASPECTS), patient arrival directly or by transfer, and time from symptom onset to initiation of IV tPA.

The meta-analysis also showed that stroke patients who were transferred for endovascular treatment had significantly longer symptom onset to endovascular hospital arrival time but significantly shorter endovascular hospital arrival to arterial puncture time when compared with direct arrival patients [17].

Rates of vessel recanalization are significantly effected by ED arrival to arterial puncture and Imaging to arterial puncture. Every additional hour between ED arrival to arterial puncture is associated with a 22% reduction in the odds of TICI 2b/3 reperfusion. Similarly, every additional hour between imaging and arterial puncture is associated with 26% reduction in the odds of TICI 2b/3 reperfusion [18]. The most likely explanation for this includes thrombus modification (higher fibrin content and more organized configuration of old thrombus compared to fresh thrombus) and stronger adhesion of the thrombus within the vessel wall over time which makes entrapment and retrieval of the thrombus more difficult [23,24].

There has been a lot of emphasis on reducing the time from stroke onset to recanalization of the occluded vessel. Recommendations have been put forth with regards to improving stroke care that starts from community education and rapid recognition of stroke symptoms, to pre-hospital assessment and care, creation of stroke centers, emergency room evaluation and stabilization, use of imaging modalities, consideration for IV thrombolysis and endovascular therapies, Get with the Guidelines (GWTG) time metrics for CT scan and IV tPA [4,25,26]. There are currently no GWTG time measures for DTP or DTR because there are many confounding variables including the availability of well-trained ED nurses, preparation of the patient for endovascular therapy (IV access, Foley catheter), rapid assembly of the endovascular team, etc. Median DTP and DTR times in SWIFT PRIME, EXTEND IA, and PENUMBRA 3D trials were 90/118; 113/156; 103/147 minutes, respectively [27–29]. Our study looked to see if faster decision-making and assembly of our NI team via institution of the Code NI alert system would improve DTP and recanalization times, which in turn may be associated with better outcomes. We did show significant improvement in all time parameters between the pre-Code NI group and Code NI group. This was likely the result of changes in multiple subprocesses which were streamlined and occurred in parallel. The more rapid availability and communication between stroke team attending, fellow, and resident reduced the decision time to call Code NI. The pre-calling of a Code NI prior to discussing the patient's case with the neurointerventionalist saved time as well because NI team members were already activated simultaneously through the operator, as opposed to personal phone calls. After hours, the preparation of the patient by the ER staff for the NI procedure saved time for the NI team so that groin puncture could be done as soon as the patient was on the table.

Limitations

There was a big difference in the number and data available for the pre-Code NI patients compared to Code NI patients. There was not adequate and consistent data available on patients who underwent a neuroendovascular procedure prior to 2012. This discrepancy effects the power of our study.

Our Code NI process had a number of limitations early on that required frequent regrouping and discussion. In the months following institution of Code NI, we found that staff required continued education with regards to the process despite initial education being given. We also found initially that despite creating an automatic paging system for the NI team, there were times that various team members did not receive their pages and so we had to have a secondary system where the operator would call the on call team members to confirm receipt of their page. Another area that needed readdressing included the ED nurses comfort with preparing the patient and in many cases, especially after hours, starting the neurointerventional procedure with the available team and remaining with the patient until the interventional nurse was available to receive handoff. To handle this issue, we created an NI kit for the ED nurse which contained pertinent supplies that the nurse may need to prepare that patient. The ED nurses were also given orientation to the biplanar angiography suite. These were just a few issues that contributed to some of the delays we found in the earlier phase of instituting Code NI.

Patient characteristics were not analyzed in this study to see if delays were confounded by individual differences

Journal of Vascular and Interventional Neurology, Vol. 19

in presentation. This review was conducted purely for process improvement purposes. A follow-up study can be done to look at such factors and include additional changes to the process.

Conclusions

As stroke treatments continue to be evaluated for utility and resultant improvements in patients' outcomes, individual hospitals and stroke teams will have to look closer at their current processes and identify areas where they can make improvements. We were able to formalize and streamline our existing process for the activation of our neurointerventional team. Our next steps include using an algorithm for rapidly identifying LVO patients to improve decision times and a further look at the individual components of our process to see where further time may be saved.

Acknowledgments:

None.

References

1. Mozzafarian D, et al. Heart disease and stroke statistics—2016 update: a report from the American Heart Association. *Circulation* 2016;133(4):e38–360.
2. Mozaffarian D, et al. Heart disease and stroke statistics—2015 update: a report from the American Heart Association. *Circulation* 2015;131(4):e29–322.
3. Saver JL. Time is brain—quantified. *Stroke* 2006;37(1):263–266.
4. Jauch EC, et al. Guidelines for the early management of patients with acute ischemic stroke: a guideline for healthcare professionals from the American Heart Association/American Stroke Association. *Stroke* 2013;44:870–947.10.1161/STR.0b013e318284056a
5. Emberson J, et al. Stroke Thrombolysis Trialists' Collaborative Group. Effect of treatment delay, age, and stroke severity on the effects of intravenous thrombolysis with alteplase for acute ischaemic stroke: a meta-analysis of individual patient data from randomized trials. *Lancet* 2014;384(9958):1929–1935.
6. Fonarow GC, et al. Improving door-to-needle times in acute ischemic stroke: the design and rationale for the American Heart Association/American Stroke Association's target: stroke initiative. *Stroke* 2011;42:2983–2989.June 25;, 2015 Available from www.heart.org/idc/groups/strokepublic/.../ucm_431317.ppt
7. Target Stroke Resources. Available from: www.targetstroke.org. http://www.strokeassociation.org/STROKEORG/Professionals/TargetStroke_UCM_314495_SubHomePage.jsp
8. Broderick JP, et al. Interventional Management of Stroke (IMS) III investigators. Endovascular therapy after intravenous t-PA versus t-PA alone for stroke. *N Engl J Med* 2013;368:893–903.
9. Berkhemer OA, et al. A randomized trial of intraarterial treatment for acute ischemic stroke. *N Engl J Med* 2015;372:11–20.
10. Goyal M, et al. Randomized assessment of rapid endovascular treatment of ischemic stroke. *N Engl J Med* 2015;372:1019–1030.
11. Campbell BCV, et al. Endovascular therapy for ischemic stroke with perfusion-imaging selection. *N Engl J Med* 2015;372:1009–1018.
12. Saver J. Solitaire FR as primary treatment for acute ischemic stroke (SWIFT PRIME). Invited Presentation. International Stroke Conference (ISC)February 12–15, 2015Nashville, TN
13. Fransen PSS, et al. Time to reperfusion and treatment effect for acute ischemic stroke: a randomized clinical trial. *JAMA Neurol* 2016;73(2):190–196.10.1001/jamaneurol.2015.3886
14. Khatri P, et al. IMS III trialists. Time to angiographic reperfusion and clinical outcome after acute ischaemic stroke: an analysis of data from the Interventional Management of Stroke (IMS III) phase 3 trial. *Lancet Neurol* 2014;13:567–574.
15. Khatri P, et al. IMS I and II investigators. Good clinical outcome after ischemic stroke with successful revascularization is time-dependent. *Neurology* 2009;73:1066–1072.
16. Nogueira RG, et al. DAWN trial investigators thrombectomy 6 to 24 hours after stroke with a mismatch between deficit and infarct. *N Engl J Med* 2018;378:11–21.10.1056/NEJMoa1706442
17. Saver JL, et al. Time to treatment with endovascular thrombectomy and outcomes from ischemic stroke: a meta-analysis. <Hyper-link>Jama. *</HYPERLINK>* 2016;316(12):1279–1288.10.1001/jama.2016.13647
18. Bourcier R, et al. Association of time from stroke onset to groin puncture with quality of reperfusion after mechanical thrombectomy. *JAMA Neurol* 2019;6:405–411.10.1001/jamaneurol.2018.4510
19. Kidwell CS, et al. MR RESCUE investigators. a trial of imaging selection and endovascular treatment for ischemic stroke. *N Engl J Med* 2013;368(10):914–923.
20. Ciccone A, et al. SYNTHESIS expansion investigators. *N Engl J Med* 2013;368(10):904–913.
21. Spokoyny I, et al. Accuracy of first recorded "last known normal" times of stroke code patients. *J Stroke Cerebrovasc Dis* 2015;24(11):2467–2473.
22. Wheeler HM, et al. The growth rate of early DWI lesions is highly variable and associated with penumbral salvage and clinical outcomes following endovascular reperfusion. *Int J Stroke* 2015;10(5):723–729.
23. Fennell VS, et al. What to do about fibrin rich "tough clots"? comparing the Solitaire stent retriever with a novel geometric clot extractor in an in vitro stroke model. *J Neurointerv Surg* 2018;10(9):907–910.
24. Laridan E, et al. Neutrophil extracellular traps in ischemic stroke thrombi. *Ann Neurol* 2017;82(2):223–232.10.1002/ana.24993
25. Vagal AS, et al. Time to angiographic reperfusion in acute ischemic stroke decision analysis. *Stroke* 2014;45:3625–3630.10.1161/STROKEAHA.114.007188
26. Khalessi AA, et al. Commentary: societal statement on recent acute stroke intervention trials: results and implications. *Neurosurgery* 2013;73:E375–E379.
27. Saver JL, et al. Swift prime investigators. Stent-retriever thrombectomy after intravenous t-PA vs. t-PA alone in stroke. *N Engl J Med* 2015;372(24):2285–2295.
28. Campbell BC, et al. Endovascular therapy for ischemic stroke with perfusion-imaging selection. *N Engl J Med* 2015;372(11):1009–1018.
29. Nogueira RG, et al. Safety and efficacy of a 3-dimensional stent retriever with aspiration-based thrombectomy vs aspiration-based thrombectomy alone in acute ischemic stroke intervention. a randomized clinical trial. *JAMA Neurol* 2018;75(3):304–311.